

FIGURE 1

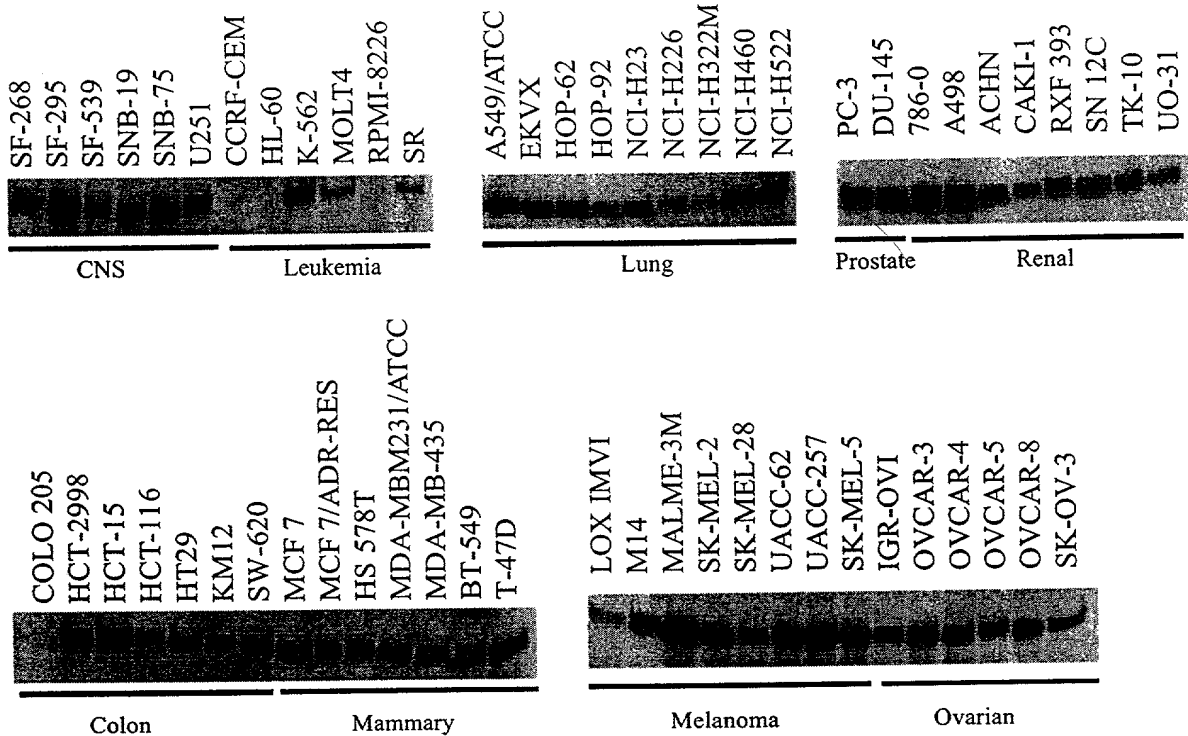


Figure 2

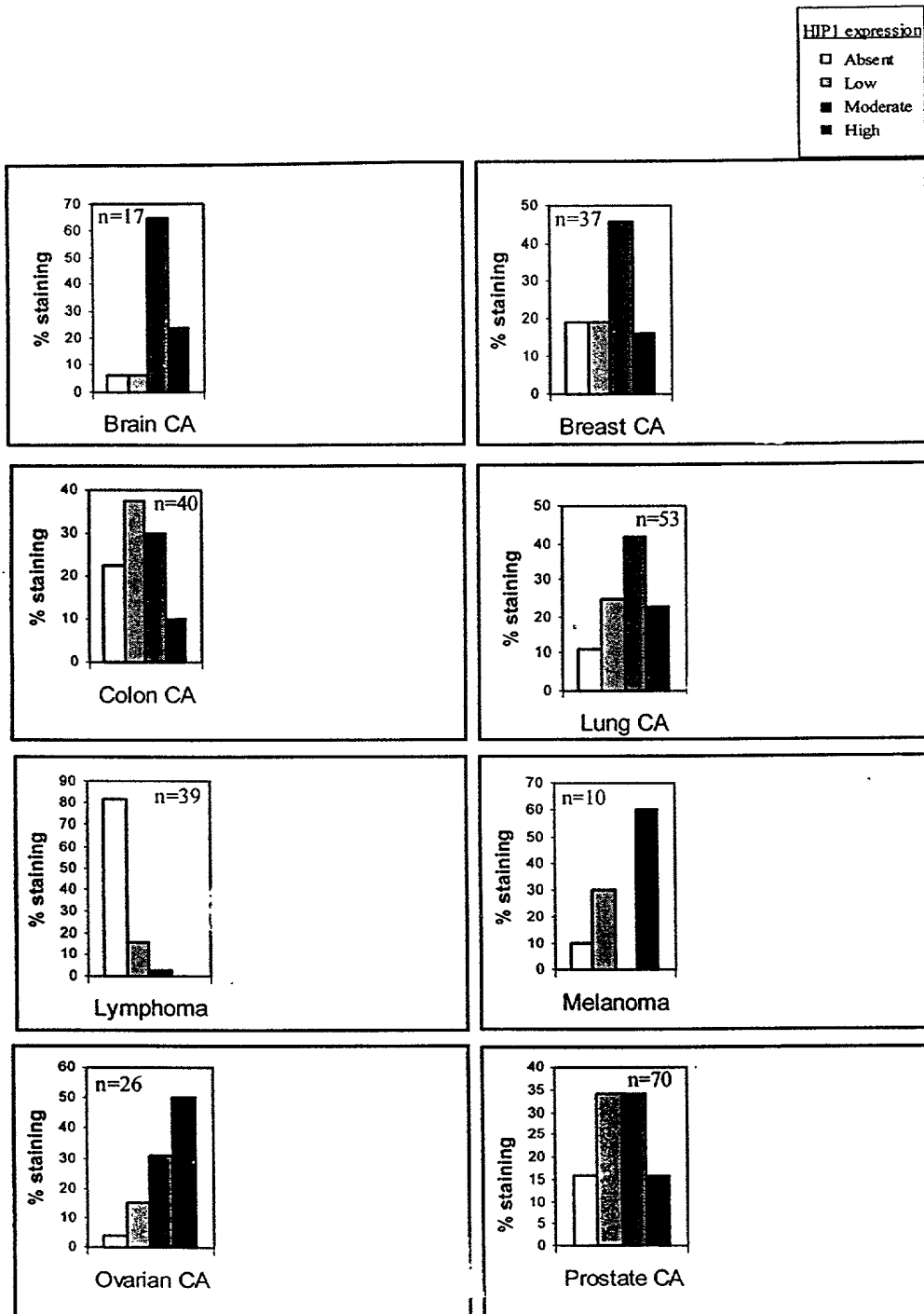
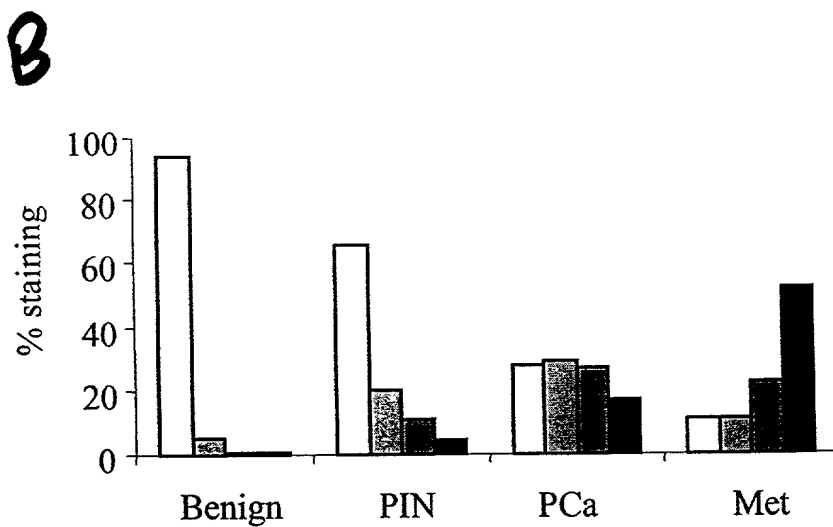
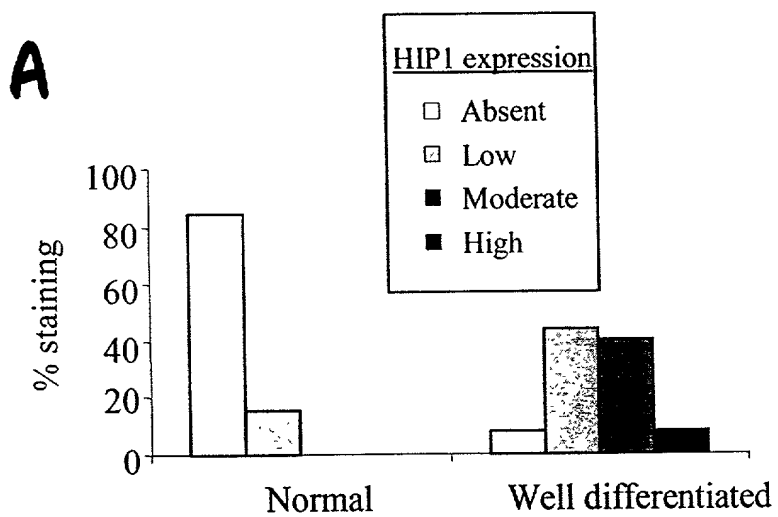


Figure 3



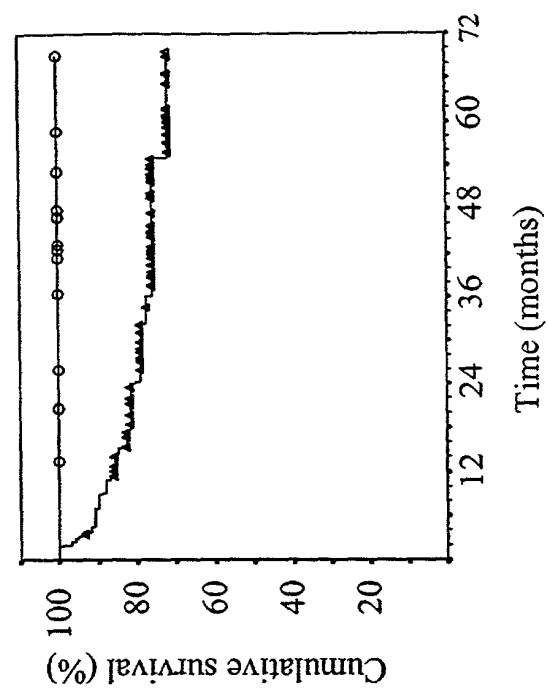
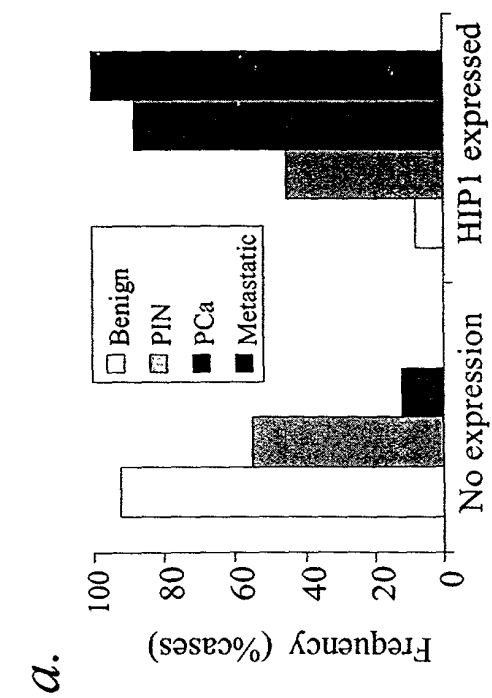


Figure 4

Figure 5

| ID # | HIP1 expression |     |          |      | Total |
|------|-----------------|-----|----------|------|-------|
|      | Absent          | Low | Moderate | High |       |
| 21   | 6               |     |          |      | 6     |
| 22   |                 | 2   |          |      | 2     |
| 23   | 1               | 1   | 1        |      | 3     |
| 25   | 1               | 3   |          |      | 4     |
| 26   |                 | 2   | 1        |      | 3     |
| 31   |                 |     | 3        | 1    | 4     |
| 32   |                 | 1   | 2        | 1    | 4     |
| 33   |                 |     |          | 2    | 2     |
| 38   | 1               |     | 1        | 4    | 6     |
| 43   |                 | 2   | 2        | 1    | 5     |
| 44   | 2               | 2   |          |      | 4     |
| 45   |                 | 2   |          |      | 2     |
| 53   |                 | 1   | 2        | 1    | 4     |
| 56   |                 |     | 2        |      | 2     |
| 58   |                 |     | 3        | 1    | 4     |
| 62   | 1               |     | 1        | 2    | 4     |
| 63   |                 |     | 5        | 1    | 6     |
| 65   | 1               | 1   | 1        | 2    | 5     |
| 66   | 1               | 1   | 1        |      | 3     |
| 67   | 2               | 1   |          | 1    | 4     |
| 70   | 2               | 1   | 2        |      | 5     |
| 73   |                 | 1   | 6        |      | 7     |
| 75   | 2               |     |          |      | 2     |
| 76   | 1               | 3   | 1        |      | 5     |
| 77   | 3               | 1   |          |      | 4     |
| 78   | 1               | 2   |          |      | 3     |
| 82   | 1               | 2   |          |      | 3     |
| 83   | 1               | 1   | 1        | 3    | 6     |
| 84   | 2               | 1   | 1        | 2    | 6     |
| 85   | 1               | 3   | 1        |      | 5     |
| 89   | 1               | 1   | 3        | 1    | 6     |
| 91   |                 |     | 4        |      | 4     |
| 92   | 1               | 1   | 1        |      | 3     |
| 93   |                 | 1   | 2        | 2    | 5     |
| 96   | 2               | 1   | 1        | 2    | 6     |
| 97   | 1               | 2   | 1        |      | 4     |
| 99   |                 |     | 2        | 2    | 4     |
| 101  |                 | 2   | 4        |      | 6     |
| 102  | 4               |     |          | 1    | 5     |
| 103  |                 | 4   |          |      | 4     |
| 105  |                 | 2   | 1        |      | 3     |
| 106  | 1               | 1   |          | 1    | 3     |
| 108  |                 | 1   | 2        | 3    | 6     |
| 109  |                 | 1   | 5        |      | 6     |
| 110  | 3               |     |          |      | 3     |
| 111  | 4               | 1   |          |      | 5     |
| 113  | 2               |     | 2        |      | 4     |
| 114  | 2               |     |          |      | 2     |
| 115  |                 |     |          | 2    | 2     |
| 117  |                 |     | 2        |      | 2     |

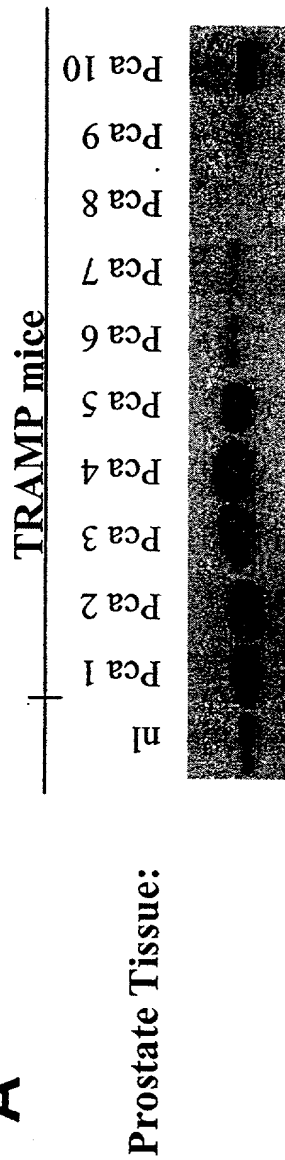
| ID # | HIP1 expression |     |          |      | Total |
|------|-----------------|-----|----------|------|-------|
|      | Absent          | Low | Moderate | High |       |
| 118  |                 | 1   | 3        |      | 4     |
| 119  |                 | 2   | 3        | 2    | 7     |
| 123  | 3               | 3   | 1        |      | 7     |
| 125  | 4               | 2   |          |      | 6     |
| 127  | 3               | 1   |          |      | 4     |
| 128  |                 |     | 1        | 3    | 4     |
| 129  | 3               | 1   |          |      | 4     |
| 131  | 1               | 1   |          |      | 2     |
| 132  |                 |     | 3        | 1    | 4     |
| 141  |                 |     | 2        | 2    | 4     |
| 142  | 2               | 3   |          |      | 5     |
| 144  | 1               | 3   | 2        | 1    | 7     |
| 145  | 2               |     |          |      | 2     |
| 153  |                 | 1   | 1        |      | 2     |
| 154  | 2               |     |          |      | 2     |
| 155  |                 |     |          | 4    | 4     |
| 159  | 4               | 2   |          |      | 6     |
| 161  | 2               |     |          |      | 2     |
| 162  | 1               | 1   | 1        |      | 3     |
| 164  |                 |     | 1        | 3    | 4     |
| 165  |                 | 4   | 2        |      | 6     |
| 169  |                 | 2   |          |      | 2     |
| 170  | 3               | 2   | 1        |      | 6     |
| 171  |                 |     | 2        |      | 2     |
| 172  | 2               |     |          |      | 2     |
| 173  | 3               |     | 1        |      | 4     |
| 175  | 3               |     |          |      | 3     |
| 177  | 4               | 2   |          |      | 6     |
| 178  | 2               | 1   |          |      | 3     |
| 179  | 3               | 1   |          |      | 4     |
| 180  | 1               |     |          | 3    | 4     |
| 181  | 4               |     |          |      | 4     |
| 182  | 2               |     |          |      | 2     |
| 183  |                 | 2   |          |      | 2     |
| 186  |                 | 4   |          |      | 4     |
| 194  | 4               | 1   |          |      | 5     |
| 194  | 2               | 1   |          |      | 3     |
| 195  | 1               | 5   | 1        |      | 7     |
| 199  |                 | 1   | 1        | 1    | 3     |
| 204  |                 | 3   | 1        |      | 4     |
| 205  |                 |     | 2        | 2    | 4     |
| 206  |                 | 6   |          |      | 6     |
| 207  |                 | 4   |          |      | 4     |
| 208  |                 |     | 3        | 1    | 4     |
| 209  |                 |     | 2        | 3    | 5     |
| 212  | 1               | 4   | 1        | 3    | 9     |
| 213  | 2               | 3   | 2        |      | 7     |
| 214  |                 | 1   | 1        | 3    | 5     |
| 217  |                 | 1   | 2        | 3    | 6     |
| 218  | 1               | 6   |          |      | 7     |

5

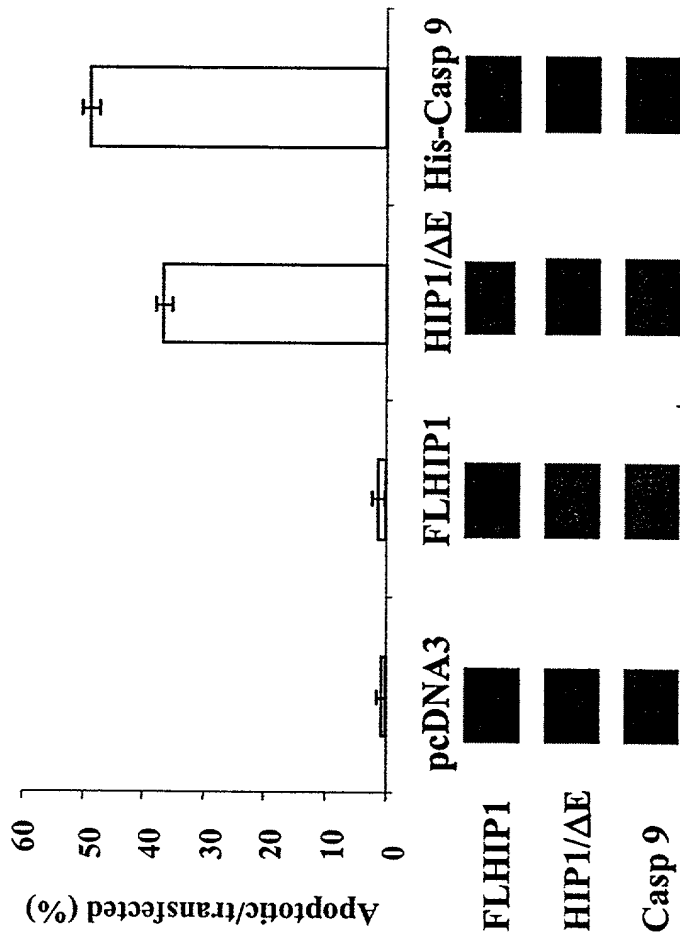
|       |     | HIP1 expression |     |          |      | Total |
|-------|-----|-----------------|-----|----------|------|-------|
|       |     | Absent          | Low | Moderate | High |       |
| ID #  | 220 |                 | 1   |          | 5    | 6     |
|       | 225 |                 | 1   | 3        |      | 4     |
|       | 228 |                 |     | 3        |      | 3     |
|       | 229 | 1               |     | 2        | 1    | 4     |
|       | 230 | 2               |     |          |      | 2     |
|       | 231 |                 |     | 2        | 1    | 3     |
|       | 234 |                 |     | 2        |      | 2     |
|       | 235 |                 | 3   | 1        |      | 4     |
|       | 236 | 2               | 3   |          |      | 5     |
|       | 237 | 4               | 1   |          |      | 5     |
|       | 238 | 2               |     |          |      | 2     |
|       | 239 |                 | 3   | 2        |      | 5     |
|       | 241 | 2               | 1   | 1        |      | 4     |
|       | 248 |                 |     | 2        |      | 2     |
| TOTAL |     | 128             | 136 | 123      | 76   | 463   |

**A**

Figure 6



**B**



**Figure 7**  
**Full length HIP1 (SEQ ID NO:1)**

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20250406

# Figure 8 Full length HIP1 (SEQ ID NO:2)

E JC162  
29 2002  
18 10 1999

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G\*VSRAPQLW\*LQRWCCPGLSVLHLRLHTDQVLAHPVHAPGSGGAAE\*QLSSKSRRRVSAFPS\*S\*IPAES  
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IPNSFLQTSALASS\*IGRSFHLLRN\*QTRKIRCNCSEQRTLYLVCYP\*YLLLTSLKQQQPTKRCLEQSEL  
QV\*L\*QSSSFCPATSAFKNQKKGQAGLLLTWIPKQGDHLELLGQRK\*ERTEPAAPTFFSHMPQALAAALWT  
G\*GQRAHEQLARDGQPNSTFPLLDGPQHLSDLLILGKQRLPSLSIATHWW\*PSSTSEFLQPRPLEHAXEG  
P

(\* are stop sequences)

**Figure 9**  
**Delta ENTH (SEQ ID NO:3)**

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gtcaggcggagctgctgagtgcagcttccctcaaaaagcagaaggagagtgagtgctttccctcctaaa  
gctgaatccggcggaagcctctgtccgcctttacaaggggagaagacaacagaaaggagggaagagggt  
tcacacagcccagttccgtgacgaggctcaaaaacttgatcacatgcttgatggagctgggtgagatcaa  
caacactacttccctgccggaatgaactgtccgtgaatgggtctctgtcaagcgggctcctccttgccc  
agagacggagtggtggagtgattcccaactcctttctgcagacgtctgccttggcatcctcttgatagga  
agatcgttccacttctacgcaattgacaaaccggaagatcagatgcaattgctcccatcaggaagaac  
cctatacttggttgctacccttagtatttattactaacctcccttaagcagcaacagcctacaaagagat  
gcttgagcaatcagaacttcaggtgtgactctagcaagctcatctttctgcccggctacatcagccttc



## Figure 10

### Delta ENTH (SEQ ID NO:4)

MFDYLECELNLQFQTVFNSLMSRSVSVTAAGQCRLAPLIQVILDCSHLYDYTVKLLFKLHSCLPADTLQGH  
 RDRFMEQFTKLKDLFYRSSLQYFKRLIQIPQLPENPPNFLRASALSEHISPVVVI PAEASSPDSEPVLEK  
 DDLMDMDASQQNLFDNKFDDIFGSSFSDDPFNFNSQNGVNKDEKDHLIERLYREISGLKAQLENMKTESQR  
 VVLQLKGHVSELEADLAEQQHLRQQAADDCEFLRAELDELRRQREDTEKAQRSLSEIERKAQANEQRYSKL  
 KEKYSSELVQNHADLLRKNAEVTQVSMARQAQVDLEREKKELEDSELRISDQGQRKTQEQLVLESLSKQEL  
 ATSQRELQVLQGSLETSQAQSEANWAAEFAELEKERDSLVSAGAAHREEELSALRKELQDTQLKLASTEESMC  
 QLAQDQRKMLLVGSRKAAEQVIQDALNQLEEPPLISCAGSADHLLSTVTSISSCIEQLEKSWSYLACPED  
 ISGLLHSITLLAHLTSDAIAHGATTCLRAPPEPADSLTEACKQYGRETAYLASLEEESLENADSTAMRN  
 CLSKIKAIGEELLPRGLDIQBELGDLVDKEMAATSAAIETATARIEEMLSKSRAGDTGVKLEVNERILGC  
 CTSLMQAIQVLIVASKDLQREIVESGRGTASPKFYAKNSRWTEGLISASKAVGWGATVMVDAADLVVQGR  
 GKFEELMVCSHEIAASTAQLVAASKVKADKDSPNLAQLQASRGVNQATAGVVASTISGKSQIEETDNMDF  
 SSMTLTQIKRQEMDSQVRVLELENELQKERQKLGLRKKHYELAGVAEGWEEGTEASPTLQEVVTEKE\*S  
 QTNTPYVSVNPNPCYLSRVCFPSHRPNPWSPRGSHTTAITQCRGHA\*HFQRLPP\*RHPFCLDPWISTASYGG  
 WLGLVLVFFFKFHSHSQLSQRAPWG\*VSRAPQLW\*LQRWCCPGLSVLHLRLHTDQVLAPVHAPGSGGA  
 AE\*QLSSKSRRRVSAFPS\*S\*IPAESLCPPLOQRRQKEGQEGSHSPVPVTRLKNLITCLNGAGEINNTTS  
 LPE\*TVREWSLSSGSPPLAQRRSVGVIPNSFLQTSALASS\*IGRSFHLLRN\*QTRKIRCNC SHQGR TLYLV  
 CYP\*YLLLTSLKQQQPTKRCLEQSELQV\*L\*QSSSFCPATSAFKNQKKGQAGLLLTWIPKQGDHLELLGQ  
 RK\*ERTEPAAPT PFSHMPQALAAALWTG\*GQRAHEQLARDGPNSTFPLLDGPQHLSDLLILGKQRLPSLSI  
 ATHWW\*PSSTSEFLQGRPLEH

(\* are stop sequences)

h1

Figure 11

# Domain Structure of HIP1

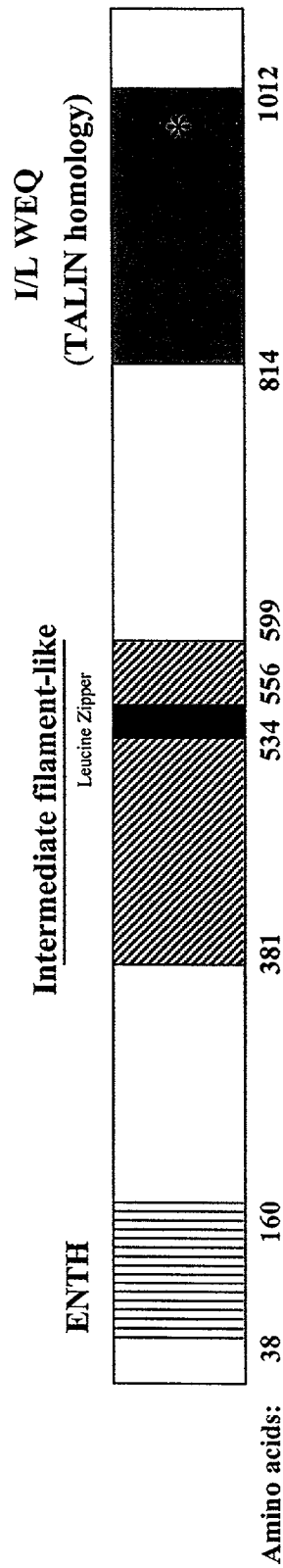
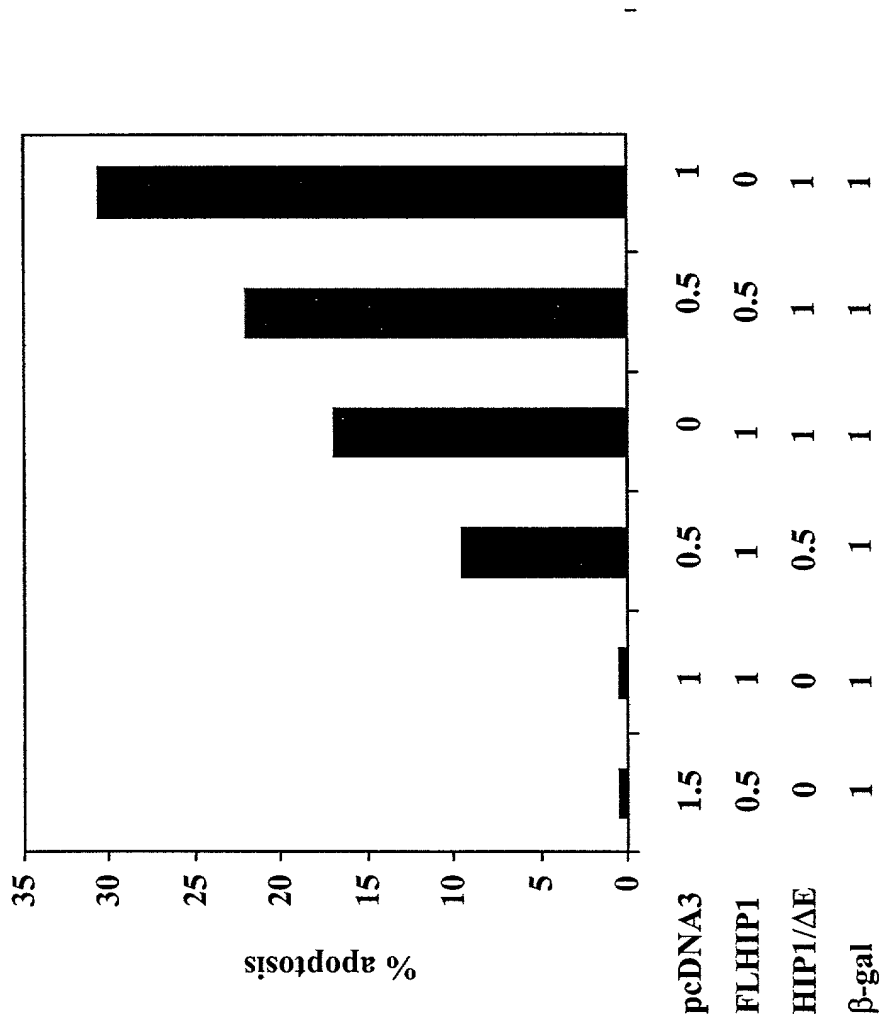


Figure 12

# Rescue of apoptosis caused by $\Delta E$ with FLHIP1



18 h post-transfection

Figure 13

# Rescue only with Akt/Dncasp9

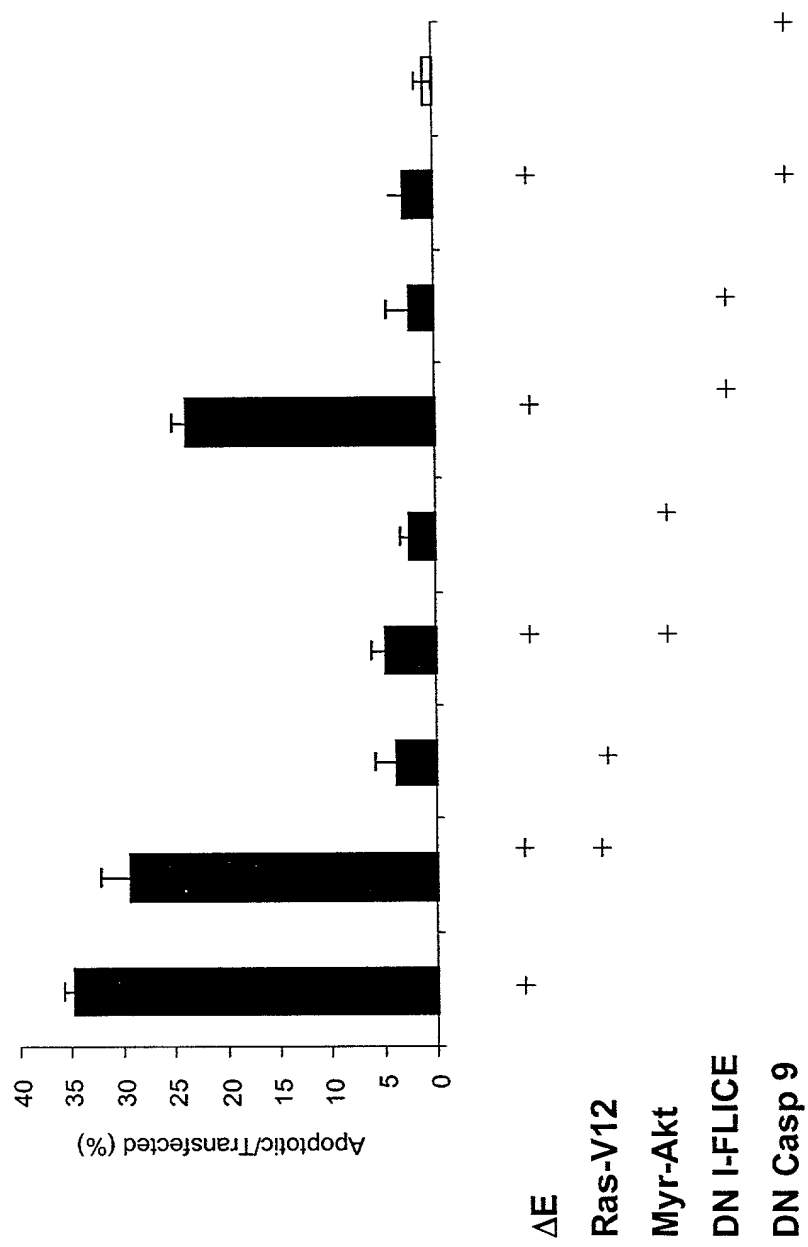


Figure 14

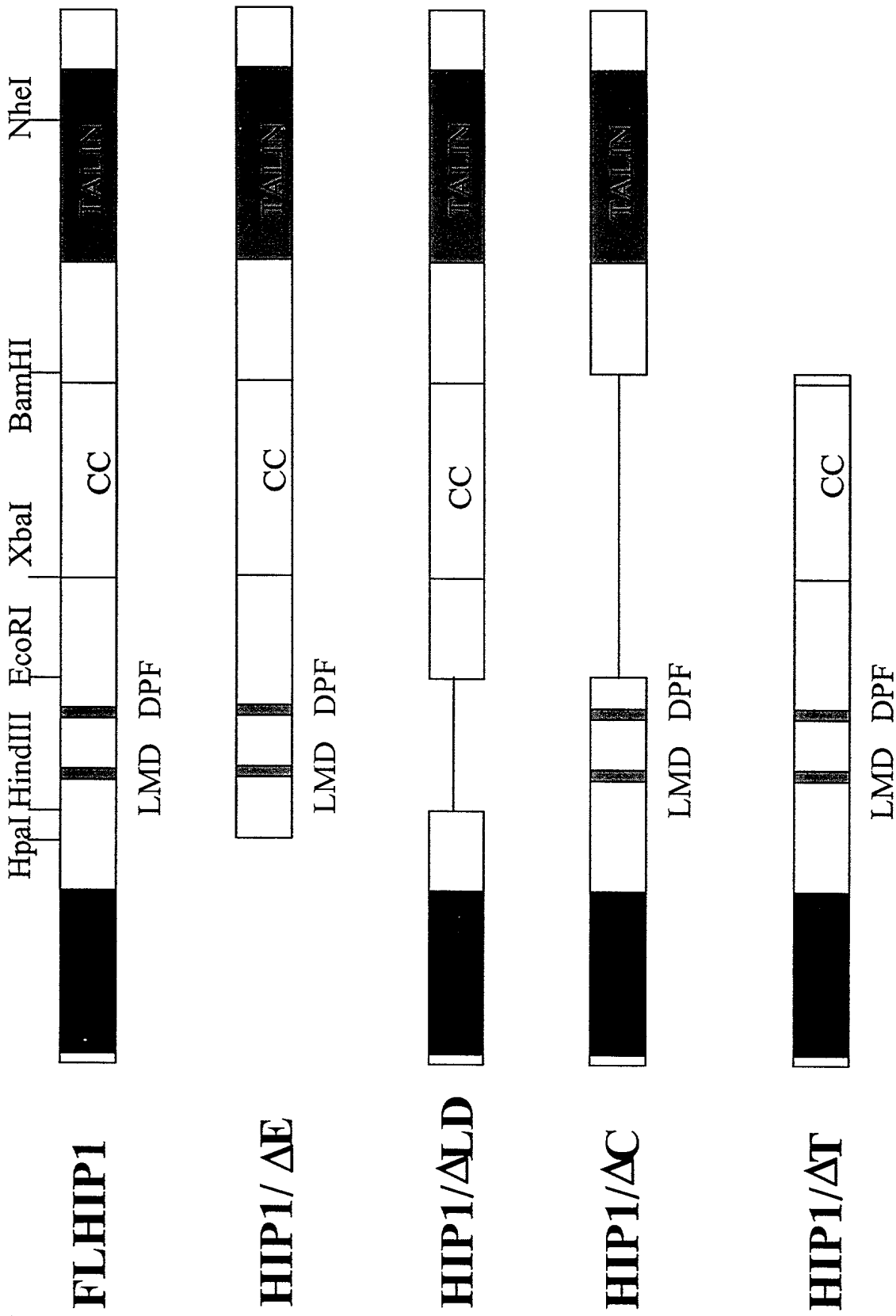
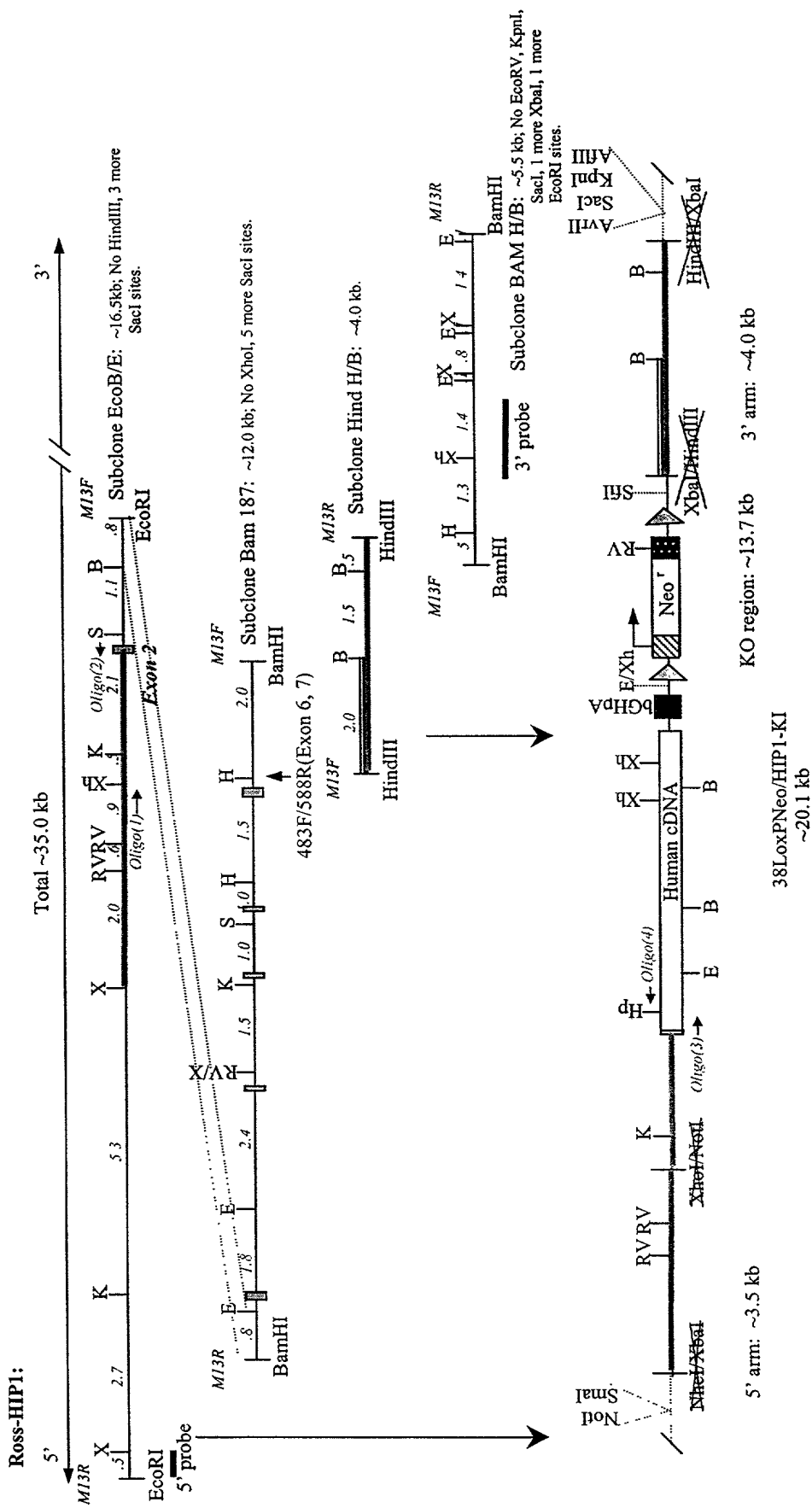


Figure 15

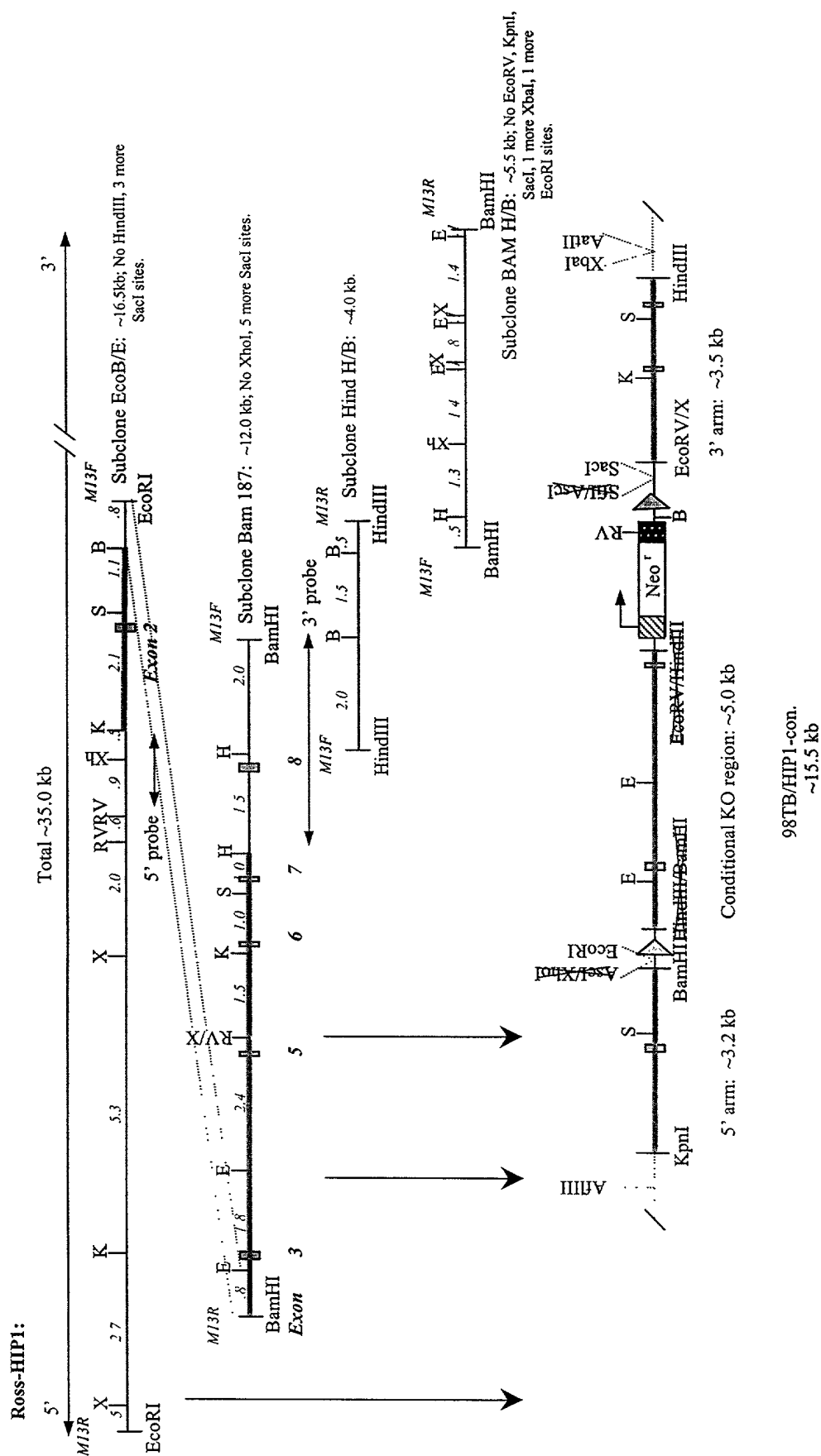
# Vector Construction Strategy for HIP1/PDGFβR knock-in



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Figure 16

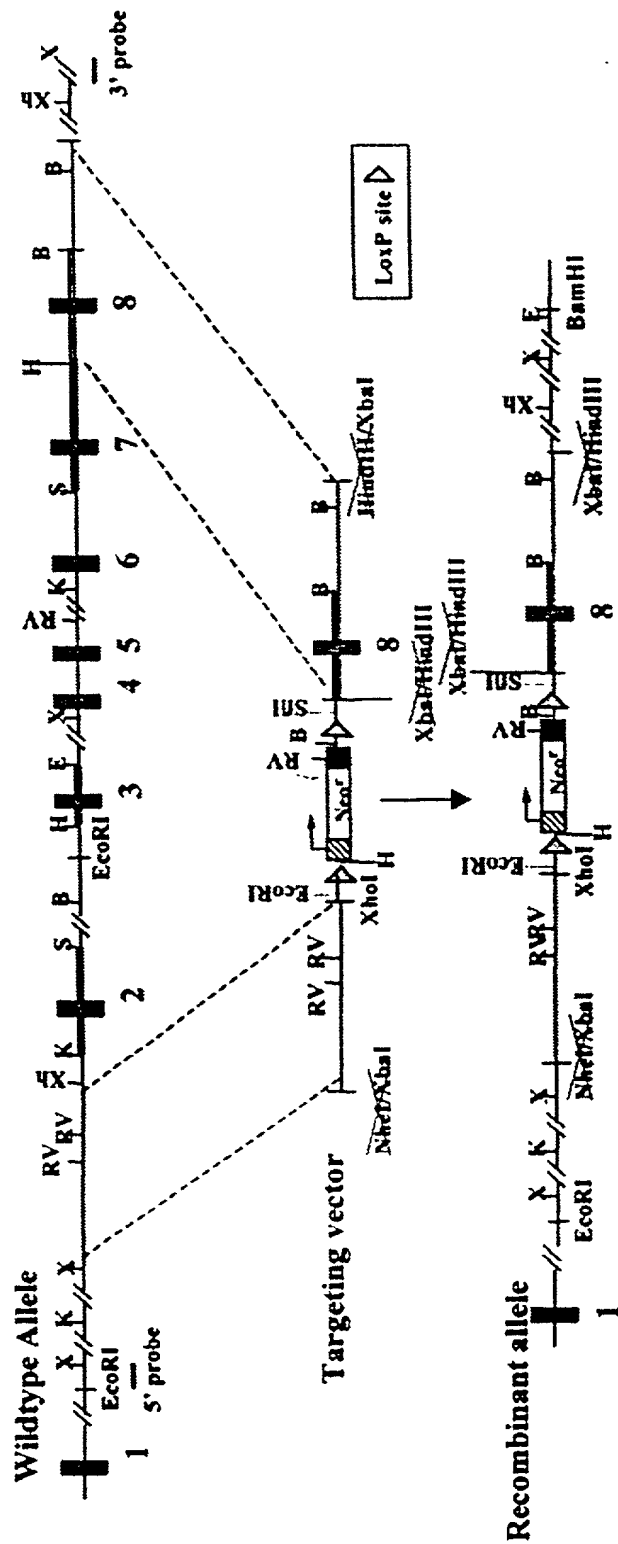
# Vector Construction Strategy for conditional HIP1 knock-out



# Figure 17

-173 GGGCCGAGCCAGCGGAGGGGCTCCTGAAGGGGCGGGGGCGGGCGGGGAAGCCGT  
 -119 TCGGCGAGGGGCGGGGTCTCTGGAAGACTGGCAGAACTCACAGCCAATGGCAGGC  
 -64 GGGAGCCGTCCCGTTAGCGCCGATCCCCGCGGGTAGGGCGGGGCGGGCGGGCGCC  
 -10 GTGGGGATCC  
 exon 1 0 CGGGGCAGCCGAGGGCCCCTGACTCGGCTCCTCGCGGCGACATGGATCGGATGGCCA  
 57 GCTCCATGAAGCAGGTGCCCAACCCACTGCCCAAGGTGCTGAGCCGGCGCGGGGTCG  
 114 GCGCTGGGCTGGAGGCGGCGGAGCGCGAGAGCTTCGAGCGGAC TCAGGT.....  
 .....TCAG  
 exon 2 161 ACTGTCAGCATCAATAAGGCCATTAATACGCAGGAAAGTGGCTGTAAAGGAAAAACATGCC  
 222 AG

Figure 18



[illegible]